UNIVERSITY OF CAMBRIDGE

NIHR | Blood and Transplant Research Unit in Donor Health and Behaviour at University of Cambridge

Gifting safely: evaluating the health impacts of voluntary blood donation

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12 June 2024

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Outline

- Why does this PhD matter?
- **Completed project**: Risk factors for blood-donation-related vasovagal reactions (VVRs): a systematic review and meta-analysis
- **Ongoing project**: Donation frequency and vasovagal reactions in English whole blood donors: associations and mechanisms
- **Planned project**: Donation frequency and cardiovascular disease in England: 12-year follow-up of a randomised trial
- Potential future analyses

Why does this PhD matter?

The need for blood

- WHO: blood + components are essential drugs
- Clinical uses include:

- Only human blood currently viable for transfusions
- Most donations voluntary in high-income countries

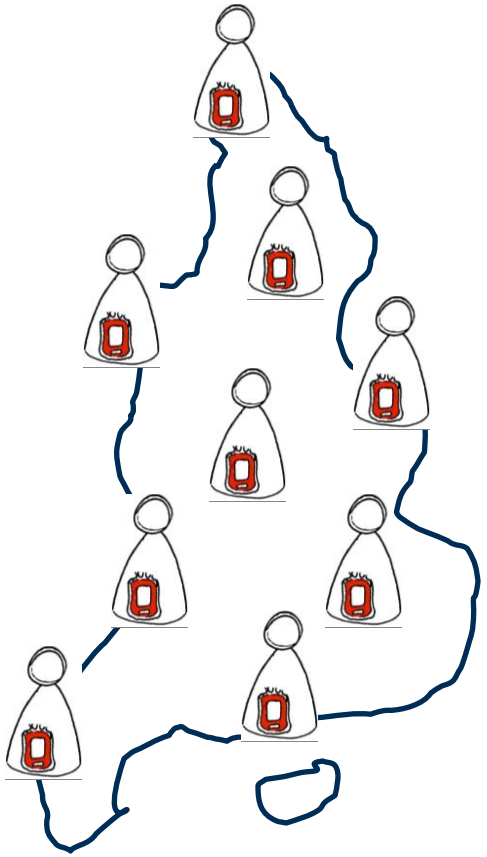
Blood donation in England

🩸 England's blood service: NHS Blood and Transplant (NHSBT)

❤️ Eligible donors are 17+ and healthy

👥 Ageing + diversifying population demands younger + BAME donors

🙋 Donor recruitment + retention = key blood service challenges



Donor safety: gaps and opportunities

Key determinant of donor participation: health impacts of donation

Donation is generally safe, but complications include:

Vasovagal reactions (one in 20)

✅ Known: potential correlates, prevention and treatment methods

❓ Gaps: risk factor validity, consistency, and mechanisms

Iron depletion (universal; differential impacts)

✅ Known: susceptible groups, potential prevention methods

❓ Gaps: long-term health impacts, including on disease risk

Risk factors for blood-donation-related vasovagal reactions (VVRs): a systematic review and meta-analysis

Background

What do we know?

VVRs (faintness/fainting) harm donor health, discourage return

Diverse individual and contextual characteristics could influence risk (via systematic + narrative reviews)

Donald et al. Transfusion (2019)

Thijsen and Masser. Transfus Med (2017)

Eder et al. Transfus Med Rev (2009)

What is missing?

Quantitative synthesis of risk factor associations

Systematic assessment of study quality (esp. for nonsyncopal VVRs)

Synthesis and evaluation of recent (post-2017) evidence

Therefore …

Methods

Searches and data extraction*

 Inception – Feb 2024

 English language studies of voluntary whole blood donors

 Design and participant characteristics, risk factor and outcome ascertainment methods

 Modified Newcastle-Ottawa Scales for voluntary donation research to assess bias

Synthesis

 Random effects meta-analysis, including dose-response meta-analysis for continuous risk factors

 Heterogeneity and subgroup differences

 Narrative synthesis for inconsistently reported risk factors

 PROSPERO: CRD42023476467

*in collaboration with Dr Hongchao Qi

Results

In 73 studies of 19 million donations,

blood donors who felt faint were often*

younger, 4.1

inexperienced, 3.9

smaller, 3.8

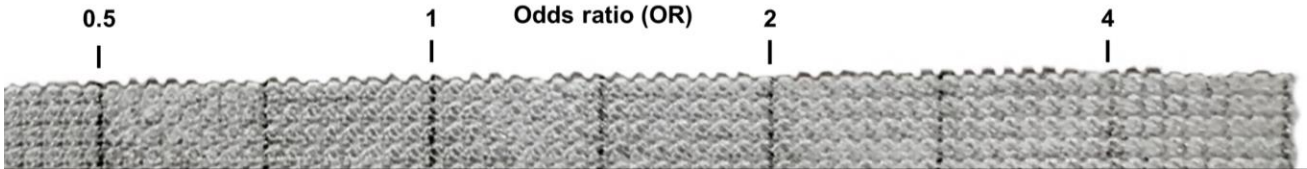
hypotensive, 2.4

female, 2.4

and fearful of donation. 2.1

2

*Random-effects-pooled unadjusted odds ratios (ORs) and 95% confidence intervals (CIs) compared binary categories for sex and new donor status and lowest and highest exposure categories for age, total blood volume, and systolic and diastolic blood pressure (all of which showed curvilinear associations in dose-response analyses). OR for donation fears was approximated from 12 narratively synthesised studies. Limited evidence was found for associations with race, heart rate, haemoglobin, and donation site type. High heterogeneity (I^2 > 90%) was observed across all risk factors, and no clear evidence for small study effects or subgroup differences was found.



Interpretation

What does this study add?

1 World-first meta-analysis of VVR risk factors across varying outcome severities and global contexts

🔍 Systematic characterisation of study quality and identification of research gaps

What else is needed?

💻 Studies using comprehensive covariate adjustment

🧬 Studies of genetic determinants

to inform 👥 the development and targeting of prevention strategies

Donation frequency and vasovagal reactions (VVRs) in English whole blood donors: associations and mechanisms

Background

What do we know?

1 Inexperienced donors are at higher VVR risk because of …

self-selection or habituation to donation stressors?

In highly motivated donors, randomised 2y donation frequency did not cause differences in blood-service-recorded VVRs

What is missing?

Evidence for associations in more population-representative samples

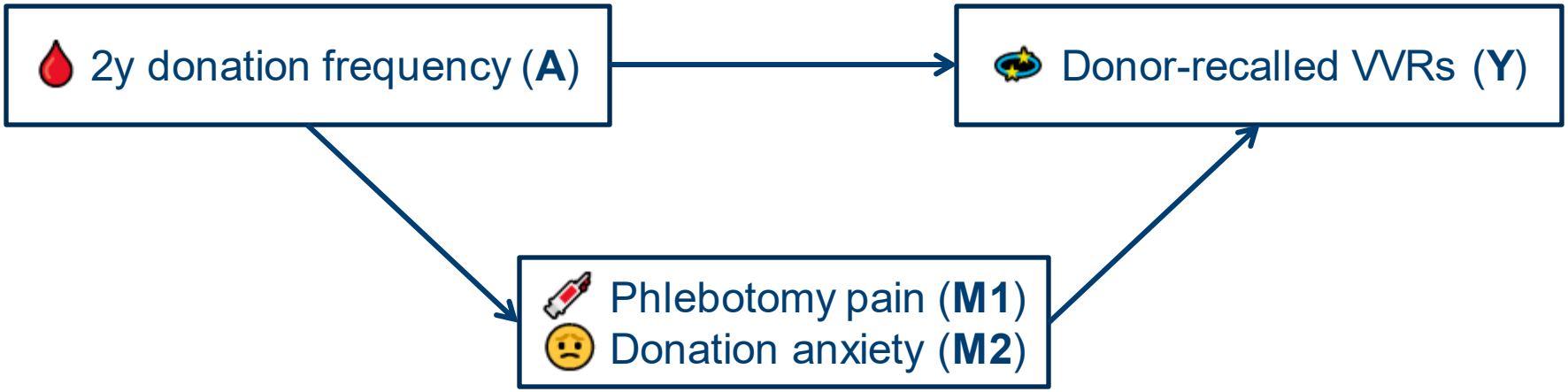
Studies measuring VVRs divorced from return behaviours

Evidence for potential mechanisms of habituation

Therefore …

Methods

STRIDES BioResource (49K 2y+ donors with no VVR history)



Mediation analyses using mediator and outcome regressions

McMahon et al. Trials (2022)

VanderWeele. Annu Rev Public Health (2016)

Results

❗ More frequent donors (2y) had **0.85x the odds** (95% CI: 0.81, 0.90) **of retrospectively-recalled VVRs** compared to less frequent donors

💉 Phlebotomy pain explained **none** of the association between donation frequency and donor-recalled VVRs, while …

😟 Donation anxiety explained **16%** of this association

Interpretation

📄 In large sample of voluntary English 2y+ donors, greater 2y🩸 donation frequency associated with lower subsequent VVR risk, with small % of association explained by 😟 anxiety

💪 Donor habituation may still occur, but mechanisms are unclear – are physiologic or behavioural factors more important?

👦⚕️ Findings motivate greater blood service vigilance for VVRs in infrequent **and** inexperienced donors alike

Next steps

- Conducting additional analyses (i.e., imputation, other outcomes)
- Writing up for thesis chapter
- Disseminating findings via conferences, journal publications

Donation frequency and cardiovascular disease in England: 12-year follow-up of a randomised trial

Background

What do we know?

🔜 Short-term complications affect some donors … evidence on aetiology, prevention growing

□ On the other hand, donation could lower cardiovascular disease risk by removing iron or thinning blood

Quee et al. Transfus Med Rev (2022)

What is missing?

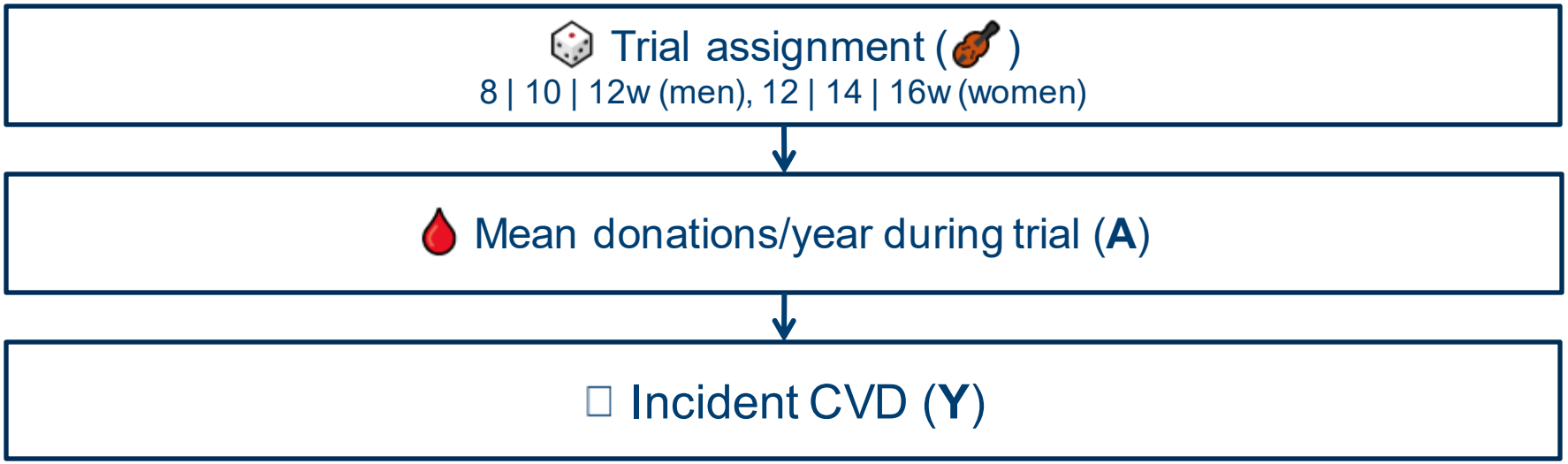
⏳ Evidence for long-term effects of donation on cardiovascular disease risk that is …

💪 robust to selection biases

Therefore …

Methods

INTERVAL trial (45K donors)



Cox models adjusted for baseline prognostic covariates

Angelantonio et al. Lancet (2017)

Impact

Inform blood service communications surrounding long-term risks (+ benefits?) of donation

Five Reasons Why You Should Donate Blood

1. Development of new red blood cells

Within the first 48 hours of blood donation, the donor's body starts replenishing the lost red blood cells. The replenishment
staying healthy and productive at work.

2. Reducing risk of heart disease

As per several studies and reports, when there is a rise in the iron level in blood, it raises the chances of heart diseases. Peop
blood from time to time in order to reduce the iron level in the blood.

3. Burns calories

Donating blood can burn approximately 650 calories for each pint that is like 450 ml of blood.

Motivate further mechanistic research

Motivate investigations in diverse populations

Potential future analyses

Short-term impacts of donation

🌡️ Quantifying influence of contextual factors, i.e., season, temperature, and donation site characteristics on VVR risk

👦🏻👦🏿 Quantifying VVR risk disparities by ethnicity and elucidating potential mechanisms

🧠 Examining potential causal links between psychiatric and neurodiverse diagnoses and VVR occurrence and reporting

Long-term impacts of donation

- Examining relationships between longer-term donation frequency and CVD risk in non-randomised samples

- Quantifying CVD risk differences in individuals with and without histories of donation-related VVRs

Thank you!

Blood stock status

Pre-Amber: O positive and negative, B negative, AB negative, A positive red cells; A negative platelets

Do something amazing
Give blood

Acknowledgements

Supervision team	Dr Lois Kim, Dr Stephen Kaptoge (advisor)
Unit leadership	Prof Emanuele di Angelantonio, Prof Angela Wood
BTRU colleagues	Dr Hongchao Qi, Dr Mifuyu Akasaki, Dr Elias Allara, Dr Spencer Keene
CEU colleagues	Dr Mat Walker, Dr Nicole Staudt, Dr Anne Forde, Dr Amy Mason, Agnieszka Egan, Ank Michielsen, Svetlana Shadrina, Hannah Lombardi
Library support	Dr Veronica Philips
Funding	National Institute of Health and Care Research
Moral support	Stelios Boulitsakis Logothetis, Nick Hirschmüller, Carmen Petitjean, Dr Aliva Salmeen
Retired + current + future donors	
Friends and family	